# Specification of Ventricular Myocyte and Pacemaker Lineages Utilizing Human Embryonic Stem Cells

## Grant Award Details

Specification of Ventricular Myocyte and Pacemaker Lineages Utilizing Human Embryonic Stem Cells

**Grant Type:** SEED Grant

**Grant Number:** RS1-00198

**Investigator:**

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| **Name:** | Sylvia Evans |
| **Institution:** | University of California, San Diego |
| **Type:** | PI |

**Disease Focus:** Heart Disease

**Human Stem Cell Use:** Embryonic Stem Cell

**Award Value:** $585,600

**Status:** Closed

## Progress Reports

**Reporting Period:** Year 2

**View Report**

## Grant Application Details

**Application Title:** Specification of Ventricular Myocyte and Pacemaker Lineages Utilizing Human Embryonic Stem Cells

**Public Abstract:**

Heart failure is a leading cause of mortality in California and the United States. Currently, there are no “cures” for heart failure.Other life threatening forms of heart disease include dysfunction of cardiac pacemaker cells, necessitating implantation of mechanical pacemakers. Although mechanical pacemakers can be efficacious, there are potential associated problems, including infection, limited battery half-life, and lack of responsiveness to normal biological cues.

Our research with human embryonic stem cells will be aimed at developing therapies for heart failure, and cardiac pacemaker dysfunction. In each of these disease settings, one might effect a “cure” by replacing worn out or dysfunctional cardiac cells with new ones. In the case of heart failure, the cells that need to be replaced are heart muscle cells, which do the majority of the work in the heart. In the case of pacemaker dysfunction, the cells that need to be replaced are pacemaker cells, a highly specialized type of heart muscle cell. To replace these cells, we need to find cells that can become heart muscle or cardiac pacemaker cells, understand how to generate fairly large numbers of them, and how to persuade them to become either heart muscle or cardiac pacemaker cells. Potential cardiac progenitor cells may come from a number of different sources, either from patients themselves, or from extrinsic sources. Regardless of the source,we need to define factors which will make the cells multiply and will make them become the cell type that we need for repair.

The biology of human heart cells is likely to be distinctive from that of heart cells from other animals. For example, a human heart has to function for multiple decades, unlike hearts of other animals who live in general for shorter periods of time. The size, required function, and rhythm of the human heart are also distinct from that of other animals. For these reasons, for repair of human heart, it is important to study human cardiac progenitors and to define pathways required to grow them and to differentiate them utilizing human cells as a model experimental system.

Our proposed research will utilize human embryonic stem cells as a source of cardiac progenitors. As human embryonic stem cells can turn into many different kinds of cells, we will create special lines of human embryonic stem cells that will become fluorescent when they adopt the cardiac progenitor, heart muscle, or pacemaker state. These lines will then be treated with a large number of small molecules to find small molecules which amplify cells the number of fluorescent cells in each of these states. The small molecules activate known biochemical pathways, so we can then use the small molecules themselves, or activate identified pathways to achieve the goal of obtaining sufficient numbers of specific cardiac cell types for cardiac therapy.

**Statement of Benefit to California:**

More Californians die each year of cardiovascular disease than from the next four leading causes of death combined. Californians continue to die or be disabled as a direct result of cardiovascular disease. Although advances in medical treatment have improved post-infarct survival, heart failure is an increasingly abundant manifestation of cardiovascular disease. A secondary complication of heart failure, and other cardiac diseases, is cardiac pacemaker dysfunction, a potentially fatal condition which is currently ameliorated by mechanical pacemakers. However, mechanical pacemakers have many associated complications,particularly for pediatric patients. For both heart failure and pacemaker dysfunction, replacement of heart muscle cells or biological pacemaker cells offers the hope of improving upon current medical practice. Our research is aimed toward developing new therapies which will allow for the replacement of these critical cell types in diseased heart.

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